

REMARKS

Claims 1-94 are pending in this application. Claims 1 and 27 have been amended to clarify the definition of variable R₁₉. Claims 20 and 31-34 have been amended to avoid use of the word "preferable" in the claims. New claims 89-93 recite certain subject matter previously identified as "preferable" in claims 20 and 31-34. New claim 94 recites a compound exemplified at page 108, Example 7Z. None of the amendments have narrowed the scope of any claims.

Applicants have also added an Abstract of appropriate length.

If there is any fee due in connection with the filing of this Preliminary Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

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GARRETT & DUNNER, L.L.P.

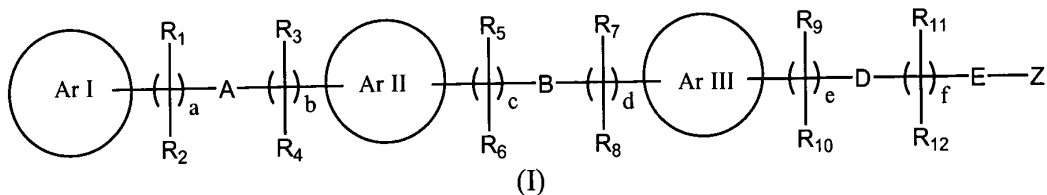
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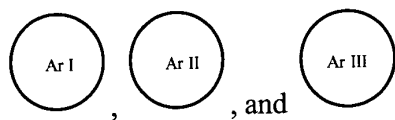
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Appendix Detailing Amendments to Claims

1. (Amended) A compound of formula I

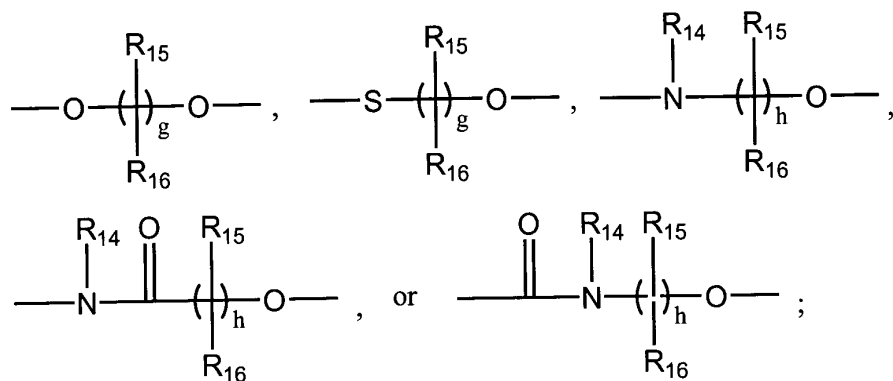


wherein:



, and are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcyloalkenyl, fused heteroarylcyloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl;

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O)-, -N(R₁₄)C(O)-, -C(O)N(R₁₅)-, -N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-, a chemical bond,



B is -O-, -S-, -SO-, -SO₂-, -NR₁₇-, a chemical bond, ethynylene, -C(O)-, -N(R₁₈)C(O)-, or -C(O)NR₁₈-;

D is -O-, -S-, -NR₁₉-, a chemical bond, ethynylene, -N(R₂₀)C(O)-, -C(O)-, or -C(O)N(R₂₀)-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R₁, R₃, R₅, R₇, R₉, and R₁₁, are independently hydrogen, halogen, alkyl, carboxyl, alkoxy carbonyl or aralkyl;

R₂, R₄, R₆, R₈, R₁₀ and R₁₂, are independently $-(CH_2)_q-X$;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl,

alkoxy carbonyl, tetrazolyl, acyl, acylHNSO₂-, -SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

Y¹ and Y² are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of

Y¹ and Y² is hydrogen or alkyl and the other of Y¹ and Y² is acyl or aroyl;

Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is R₂₁O₂C-, R₂₁OC-, cyclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-, R₂₁O- 2,4-thiazolidinedionyl, or tetrazolyl; and

[R₁₉ and] R₂₁ is [are independently] hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxy carbonyl;

or R₁₄, and R₁₅ taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

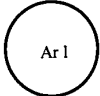
when a is 2-4, then vicinal R₁ radicals taken together with the carbon atoms to which the R₁ radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R₃ radicals taken together with the carbon atoms to which the R₃ radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R₅ radicals taken together with the carbon atoms to which the R₅ radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R₇ radicals taken together with the carbon atoms to which the R₇ radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R₉ radicals taken together with the carbon atoms to which the R₉ radicals are linked form an ethylene group; or
when f is 2-6, then vicinal R₁₁ radicals taken together with the carbon atoms to which the R₁₁ radicals are linked form an ethylene group; and
R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or
a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

20. (Amended) A compound according to claim 1 wherein  is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, *N*-alkyl-quinolin-4-onyl, quinazolin-4-onyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, indolinyl oxazolyl, thiazolyl, oxadiazolyl isoxazolyl, imidazolyl, pyrazol-yl, thiadiazolyl, triazolyl, pyridyl pyrimidinyl, pyrazinyl, pyridazinyl, phenyl, or naphthalenyl group, wherein the substituent is a ring system substituent [as defined herein, more preferably a substituent selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, lower alkyl, branched alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy].

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R₁, R₃, R₅, R₇, R₉, and R₁₁, are independently hydrogen, halogen, alkyl, carboxyl, alkoxy carbonyl or aralkyl;

R₂, R₄, R₆, R₈, R₁₀ and R₁₂, are independently -(CH₂)_q-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl,

alkoxy carbonyl, tetrazolyl, acyl, acylHNSO₂-, -SR₂₃, Y¹Y²N- or Y³Y⁴NCO-;

Y¹ and Y² are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of

Y¹ and Y² is hydrogen or alkyl and the other of Y¹ and Y² is acyl or aroyl;

Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is R₂₁O₂C-, R₂₁OC-, cyclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-, R₂₁O- 2,4-thiazolidinedionyl, or tetrazolyl;

R' and R'' are ring system substituents;

[R₁₉ and] R₂₁ is [are independently] hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxy carbonyl;

or R₁₄, and R₁₅ taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R₁ radicals taken together with the carbon atoms to which the R₁ radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R₃ radicals taken together with the carbon atoms to which the R₃ radicals are linked form an ethylene group; or
when c is 2-4, then vicinal R₅ radicals taken together with the carbon atoms to which the R₅ radicals are linked form an ethylene group; or
when d is 2-5, then vicinal R₇ radicals taken together with the carbon atoms to which the R₇ radicals are linked form an ethylene group; or
when e is 2-4, then vicinal R₉ radicals taken together with the carbon atoms to which the R₉ radicals are linked form an ethylene group; or
when f is 2-6, then vicinal R₁₁ radicals taken together with the carbon atoms to which the R₁₁ radicals are linked form an ethylene group; and
R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or
a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

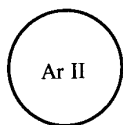
31. (Amended) A compound according to claim 27 wherein

a = 1 or 2;

A is -O-;

b = 0;

R₁, R₂, R₇ and R₈ are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, halo or benzyloxy;

R'' is lower alkyl [, preferably methyl];

Z is -CO₂H.

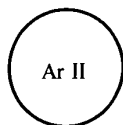
32. (Amended) A compound according to claim 27 wherein:

a = 1 or 2;

A is -O-;

b = 0;

R₁, R₂, R₅ and R₆ are independently hydrogen;



is optionally substituted phenyl;

c = 1;

B is -O-;

d = 0;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, halo or benzyloxy;

R" is lower alkyl [, preferably methyl];

Z is -CO₂H.

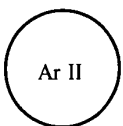
33. A compound according to claim 27 wherein:

a = 1 or 2;

A is -O-;

b = 0;

R₁, R₂, R₇, R₈, R₁₁ and R₁₂ are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

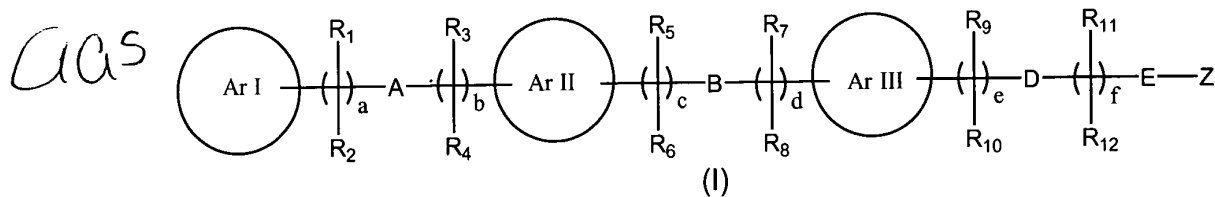
f = 1;
D and E are a chemical bond;
R' is halo;
R'' is lower alkyl [, preferably methyl];
Z is -CO₂H.

34. (Amended) A compound according to claim 27 wherein:

a = 1;
A is -O-;
b = 0;
c = 0-1;
B is -O-;
d = 0 or 1, wherein c+d = 1 or 2;
e = 0;
f = 0;
D and E are a chemical bond;
R' is hydrogen, aralkoxy, or halo;
R'' is lower alkyl [, preferably methyl];
Z is -CO₂H.

Abstract

The use of triaryl acid derivatives of formula (I)



and their pharmaceutical compositions as PPAR ligand receptor binders. The PPAR ligand receptor binders of this invention are useful as agonists or antagonists of the PPAR receptor.